

Computer Simulation of ErbB Signaling in Grid Environment

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We developed a stoichiometric simulation program includes a parameter estimator, YAGNS (Yet Another Gene Network Simulator), in our laboratory. The program solves biochemical ordinary differential equations that are automatically formed from the inputs, and displays various time-course data in graphs. For the estimation of unknown parameters, a newly developed genetic algorithm (GA) named DIDC (a genetic algorithm with Distance Independent Diversity Control) was used. Under this simulation environment, we constructed a mathematical simulation model of ligand-induced ErbB4 receptor signaling to understand the regulation mechanism in this cascade. The model well reflected the experimental results observed in ErbB4-expressing cells and in other modes of growth hormone-induced cell signaling that involve Raf-Akt cross-talk. The model suggested that HRG signaling is regulated by a protein phosphatase 2A (PP2A) as well as Raf-Akt cross-talk, and PP2A modulates the kinase activity in both the PI3K-Akt and Raf-MEK-ERK pathways. Now YAGNS is available in OBiGrid (Open Bioinformatics Grid) at <https://access.obigrid.org/yagns/> where the parallel computation enables the parameter estimation and biological simulation in a secure environment.